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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/625,559

07/24/2003

Ludwig Zorn

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EXAMINER

HANLEY, SUSAN MARIE

ART UNIT

PAPER NUMBER

1651

MAIL DATE

DELIVERY MODE

07/11/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Supplemental
Notice of Allowability

Application No.

10/625,559

Examiner

Susan Hanley

Applicant(s)

ZORN ET AL.

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 6/18/07.
2. ☒ The allowed claim(s) is/are 1-10.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>20070619</u> . |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

SUPPLEMENTAL EXAMINER'S AMENDMENT

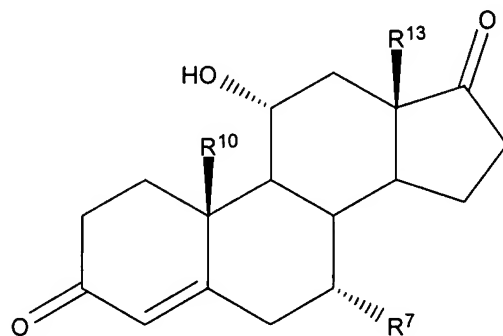
An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Anthony Zelano on 6/18/07.

IN THE SPECIFICATION:

Page 4, lines 9-16, was replaced with the following:

-- The problem on which this invention is based is solved by microbiological processes for the production of 7 α -substituted steroids as follows:
microbiological process for the production of 7 α -substituted 11 α -hydroxy steroids with general formula **4,B**:

**4,B**

in which

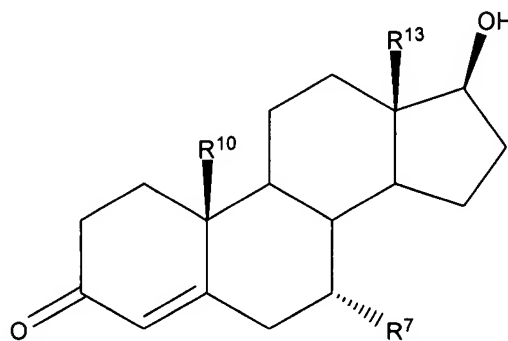
R⁷ is the grouping P-Q, whereby
P represents a C₁- to C₄-alkylene, and Q represents a C₁- to C₄-alkyl- or C₁- to C₄-fluoroalkyl, and the grouping P-Q is bonded via P to the steroid skeleton,

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R^{10} can be in α - or β -position and stands for H, CH_3 or CF_3 , and

R^{13} is methyl or ethyl,

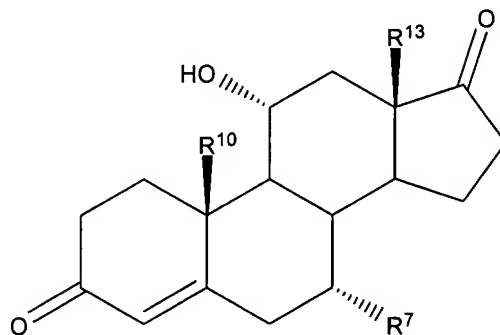
in which a 7α -substituted steroid with general formula **3,A**:

**3,A**

in which R^7 , R^{10} and R^{13} have the same meanings as indicated above,

is hydroxylated and oxidized with use of a microorganism that is selected from the group that comprises *Aspergillus sp.*, *Beauveria sp.*, *Glomerella sp.*, *Gnomonia sp.*, *Haplosporella sp.* and *Rhizopus sp.*;

microbiological process for the production of 7α -substituted 11α -hydroxy steroids with general formula **4,B**:

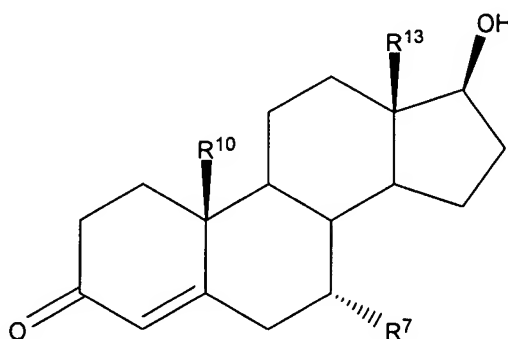
**4,B**

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in which

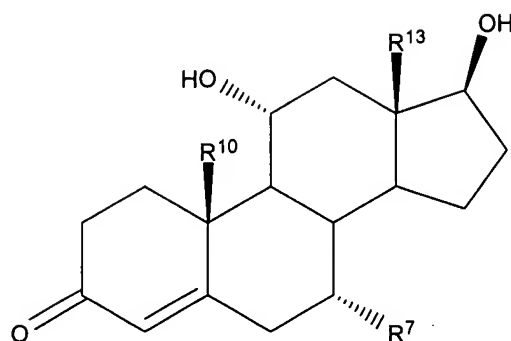
 R^7 is the grouping P-Q, whereby

P represents a C₁- to C₄-alkylene and Q represents a C₁- to C₄-alkyl- or C₁- to C₄-fluoroalkyl, and the grouping P-Q is bonded via P to the steroid skeleton,

 R^{10} can be in α - or β -position and stands for H, CH₃ or CF₃, and R^{13} is methyl or ethyl,in which a 7 α -substituted steroid with general formula 3,A:**3,A**in which R^7 , R^{10} and R^{13} have the same meanings as previously indicated,

is hydroxylated in 11 α -position in a first microbiological process step with use of a first microorganism that is selected from the group that comprises *Aspergillus sp.*, *Beauveria sp.*, *Gibberella sp.*, *Glomerella sp.*, *Gnomonia sp.*, *Metarrhizium sp.*, *Nigrospora sp.*, *Rhizopus sp.* and *Verticillium sp.*, with the formation of a 7 α -substituted 11 α -hydroxy steroid with general formula C:

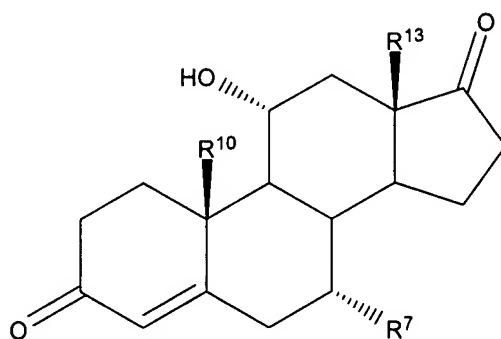
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**C**

in which R^7 , R^{10} and R^{13} have the same meanings as indicated above, and

the 7α -substituted 11α -hydroxy steroid with general formula **C** that is produced is then oxidized in a second microbiological process step with use of a second microorganism that is selected from the group that comprises *Bacillus sp.*, *Mycobacterium sp.*, *Nocardia sp.* and *Pseudomonas sp.*, with the formation of the 7α -substituted steroid with general formula **4,B**;

microbiological process for the production of 7α -substituted 11α -hydroxy steroids with general formula **4,B**:

**4,B**

in which

R^7 is the grouping P-Q, whereby

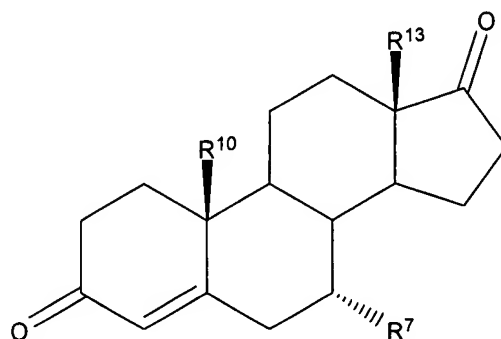
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P represents a C₁- to C₄-alkylene and Q represents a C₁- to C₄-alkyl- or C₁- to C₄-fluoroalkyl, and the grouping P-Q is bonded via P to the steroid skeleton,

R¹⁰ stands for H, CH₃ or CF₃, and

R¹³ is methyl or ethyl,

in which 7 α -substituted steroids with general formula **D**:

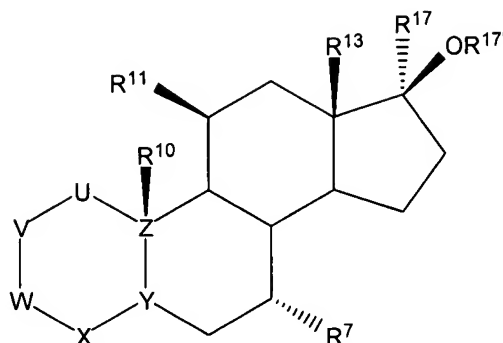
**D**

in which **R**⁷, **R**¹⁰ and **R**¹³ have the same meanings as indicated above,

are hydroxylated with use of a microorganism that is selected from the group that comprises *Aspergillus sp.*, *Beauveria sp.*, *Curvularia sp.*, *Gibberella sp.*, *Glomerella sp.*, *Gnomonia sp.*, *Haplosporella sp.*, *Helicostylum sp.*, *Nigrospora sp.*, *Rhizopus sp.* and *Syncephalastrum sp.*;

7 α ,17 α -Substituted 11 β -halogen steroids with general formulas **8**, **10**, and **12**:

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**8,10,12**

in which

U-V-W-X-Y-Z stands for one of ring structures $C^1-C^2-C^3-C^4=C^5-C^{10}$, $C^1-C^2-C^3-C^4-C^5=C^{10}$ or $C^1-C^2-C^3-C^4-C^5-C^{10}$, whereby in this case, an oxo group (=O) is bonded to W (=C³), or for ring structure $C^1=C^2-C^3=C^4-C^5=C^6$, whereby in this case radical OR³ is bonded to W (=C³),

R³ stands for H, C₁- to C₄-alkyl, C₁- to C₄-alkanoyl or a cyclic C₃- to C₇-ether with

the O-atom of the OR³-radical,

R⁷ is the grouping P-Q, whereby

P represents a C₁- to C₄-alkylene and Q represents a C₁- to C₄-alkyl- or C₁- to C₄-fluoroalkyl, and grouping P-Q is bonded via P to the steroid skeleton,

R¹⁰ can be in α- or β-position and stands for H, CH₃ or CF₃, and is present only if

X-Y-Z is not $C^4-C^5=C^{10}$,

R¹¹ is a halogen,

R¹³ is methyl or ethyl,

R¹⁷ stands for H, C₁- to C₁₈-alkyl, alicyclic C₁- to C₁₈-alkyl, C₁- to C₁₈-alkenyl,

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alicyclic C₁- to C₁₈-alkenyl, C₁- to C₁₈-alkinyl, C₁- to C₁₈-alkylaryl, C₁- to C₈-alkylenitrile or for the grouping P-Q, whereby the grouping P-Q has the above-mentioned meaning,

R^{17'} stands for H, C₁- to C₁₈-alkyl, alicyclic C₁- to C₁₈-alkyl, C₁- to C₁₈-alkenyl,

alicyclic C₁- to C₁₈-alkenyl, C₁- to C₁₈-alkinyl or C₁- to C₁₈-alkylaryl, whereby **R^{17'}** also can be bonded via a keto group to the 17β-oxy group, and whereby **R^{17'}** also in addition can be substituted with one or more groups **NR¹⁸R¹⁹** or one or more groups **SO_xR²⁰**, whereby x = 0, 1 or 2 and **R¹⁸**, **R¹⁹** and **R²⁰** in each case independently of one another can have the same meaning as **R¹⁷**,

as well as their pharmaceutically compatible addition salts, esters and amides;

process for the production of 7α,17α-substituted 11β-halogen steroids as follows:

process for the production of 7α,17α-substituted 11β-halogen steroids with general formula **10** in which U-V-W-X-Y-Z stands for the ring structure C¹-C²-C³-C⁴=C⁵-C¹⁰, with the following process steps:

- Nucleophilic substitution in a 7α-substituted 11α-hydroxy steroid with general formula **4,B** in 11-position with a halodehydroxylating reagent;
- Reaction of the 7α-substituted 11β-halogen steroid that is produced in this case with an alkylating agent in a selective manner on the C¹⁷ atom of the ring skeleton to form the 7α,17α-substituted 11β-halogen steroid with general formula **10**;

process for the production of 7α,17α-substituted 11β-halogen steroids with general formula **12** in which

U-V-W-X-Y-Z stands for the ring structure C¹-C²-C³-C⁴-C⁵=C¹⁰, with the following process steps:

- Nucleophilic substitution in a 7α-substituted 11α-hydroxy steroid with general formula **4,B** in 11-position with a halodehydroxylating reagent,
- Reaction of the 7α-substituted 11β-halogen steroid that is produced in this case with an alkylating agent in a selective manner on the C¹⁷ atom of the ring skeleton to form the 7α,17α-substituted 11β-halogen steroid with general formula **10**,

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- Isomerization of the $7\alpha,17\alpha$ -substituted 11β -halogen steroid with general formula **10** to form the corresponding isomer with general formula **12**, in which U-V-W-X-Y-Z stands for the ring structure $C^1-C^2-C^3-C^4-C^5=C^{10}$;
process for the production of $7\alpha,17\alpha$ -substituted 11β -halogen steroids with general formula **8** in which U-V-W-X-Y-Z stands for the ring structure $C^1=C^2-C^3=C^4-C^5=C^6$ with the following process steps:

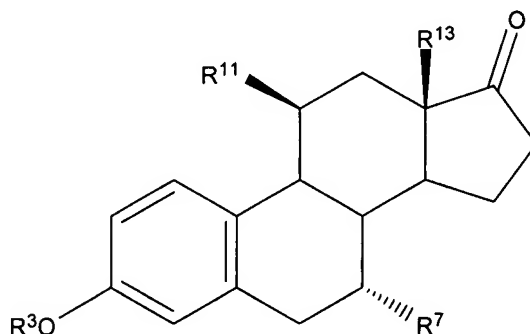
- Nucleophilic substitution in a 7α -substituted 11α -hydroxy steroid with general formula **4,B** in 11-position with a halodehydroxylating reagent,
 - Oxidizing of the 7α -substituted 11β -halogen steroid that is produced in this case to form 7α -substituted estra-1,3,5(10)-triene with general formula **6**;
 - Reaction of the 7α -substituted estra-1,3,5(10)-triene with general formula **6** with an alkylating agent in a selective manner on the C^{17} atom of the ring skeleton to form the $7\alpha,17\alpha$ -substituted 11β -halogen steroid with general formula **8**;
- use of the $7\alpha,17\alpha$ -substituted 11β -halogen steroids with general formulas **8**, **10**,

and

12 for the production of pharmaceutical agents;

pharmaceutical preparations that contain at least one $7\alpha,17\alpha$ -substituted 11β -halogen steroid with general formulas **8**, **10**, and **12** as well as at least one pharmaceutically compatible vehicle;

as well as 7α -Substituted 11β -haloestra-1,3,5(10)-trienes with general formula **6**:



6

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in which

R^3 stands for H, C_1 - to C_4 -alkyl, C_1 - to C_4 -alkanoyl or a cyclic C_3 - to C_7 -ether with

the O-atom of the OR^3 -radical,

R^7 is the grouping P-Q, whereby

P represents a C_1 - to C_4 -alkylene and Q represents a C_1 - to C_4 -alkyl- or C_1 - to C_4 -fluoroalkyl, and the grouping P-Q is bonded via P to the steroid skeleton,

R^{11} is a halogen;

R^{13} is methyl or ethyl,

as well as their pharmaceutically compatible addition salts, esters and amides. --

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508.

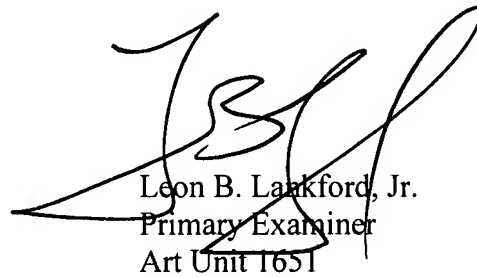
The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Susan Hanley
Patent Examiner
AU 1651



Leon B. Lankford, Jr.
Primary Examiner
Art Unit 1651